

AMENDMENTS TO THE CLAIMS

1-25. (Canceled)

26. (Currently amended) An apparatus for detecting a single nucleotide by Raman spectroscopy comprising:

a) a reaction chamber;

b) a first channel in fluid communication with the reaction chamber;

c) a second channel in fluid communication with the first channel;

d) ~~a hot spot having a three-dimensional porous structure, the hot spot being stationary within the second channel and comprising a plurality of cross-linked nanoparticle aggregates affixed within the hot spot within the second channel, wherein the three-~~
dimensional porous structure comprising a hot spot that enhances a Raman signal of the
single nucleotide; and

e) a Raman detector operably coupled to the second channel to detect the single nucleotide,

wherein the plurality of cross-linked nanoparticles aggregates affixed within the hot spot within second channel are packed and crosslinked to form the three-dimensional porous structure of the hot spot within the second channel;.

27. (Canceled)

28. (Canceled)

29. (Previously Presented) The apparatus of claim 26, wherein the first channel is a microfluidic channel.

30. (Previously Presented) The apparatus of claim 26, wherein the second channel is a nanochannel or a microchannel.

31. (Previously Presented) The apparatus of claim 26, wherein the plurality of cross-linked nanoparticle aggregates comprise between two to six nanoparticles per aggregate.

32. (Previously Presented) The apparatus of claim 26, wherein the plurality of cross-linked nanoparticle aggregates comprise two nanoparticles per aggregate.

33. (Previously Presented) The apparatus of claim 31, wherein the plurality of cross-linked nanoparticle aggregates comprise gold and/or silver nanoparticles, and the nanoparticles are between about 1 nm and 2 μ m in size.

34. (Previously Presented) The apparatus of claim 26, wherein the plurality of cross-linked nanoparticle aggregates affixed within the second channel are throughout a cross sectional area of the second channel and the Raman detector is adapted to detect said Raman signal.

35. (Previously Presented) The apparatus of claim 26, wherein the reaction chamber comprises an exonuclease.

36. (Previously Presented) The apparatus of claim 26, wherein the single nucleotide is a single unlabeled nucleotide.

37. (Previously Presented) The apparatus of claim 26, wherein the single nucleotide is a single Raman labeled nucleotide.

38. (Previously Presented) The apparatus of claim 26, further comprising electrodes positioned to create a field to guide the single nucleotide from the first channel into the second channel such that nucleotides pass through the hot spot.